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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

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Applicant's or agent's file reference 100886-1 WO				FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)				PEA/416)
Inter	national	applic	ation No.	International filing date (da	y/month/yea	ar)	Priority date (day/month/yea	ir)
PCT/SE 03/01703				05.11.2003			07.11.2002	
Inter	national	Paten	t Classification (IPC) or bo	oth national classification and	IPC			
	C07D295/155							
•								
A	laant.							
	Applicant ASTRAZENECA AB et al.							
1.	This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.							
2.	This	REPO	ORT consists of a total	of 5 sheets, including this	s cover sh	eet.		
		Thie	ronort is also accomna	nied by ANNEXES, i.e. s	heets of th	e descriptio	on, claims and/or drawings	s which have
ļ	<u> </u>	hoor	amended and are the	basis for this report and/o	or sheets c	ontaining re	ectifications made before	this Authority
1	٠	(see	Rule 70.16 and Section	n 607 of the Administrativ	e instructi	ons unuer t	sie POT).	
ļ	Thes	e anr	nexes consist of a total	of sheets.				
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			tt-i idiagliana v	alating to the following ito	me:			
3.	Inis	repor	t contains indications re	elating to the following ite	1115.			ļ
 .	1 .	\boxtimes	Basis of the opinion		•			
1	H		Priority				the state of the s	
III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability								
1	IV		Lack of unity of inven		1		wantiwa atan ar industrial	applicability:
	V	×	Reasoned statement citations and explana	under Rule 66.2(a)(ii) wit itions supporting such sta	n regard to tement	o noveity, ir	nventive step or industrial	applicability,
İ	VI		Certain documents ci	ited				
	VII		Certain defects in the	international application				
	VIII		Certain observations	on the international appli	cation			
	4- of our	mical	on of the demand		Date of co	mpletion of t	this report	
Date of submission of the demand				D uio 0, 00	///pio.io// 0. (
14	14.05.2004			15.12.2004				
Na	Name and mailing address of the international preliminary examining authority:			Authorize	d Officer		distant Peterseny.	
European Patent Office					_			
	<i>6</i>)		-80298 Munich el. +49 89 2399 - 0 Tx: 523	3656 enmu d	Usuelli,			
-	<u> </u>		ax: +49 89 2399 - 4465	while a	Telephon	e No. +49 89	2399-7366	Sporting sound .
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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/SE 03/01703

I.	Basis	of the	ne re	port
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1. With regard to the **elements** of the international application (Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)):

	Description, Pages						
	1-35	5	as published				
	.			•			
	Clai	ms, Numbers					
	1-12		as published				
2.	. With regard to the language , all the elements marked above were available or furnished to this Authority language in which the international application was filed, unless otherwise indicated under this item.						
	The	se elements were ava	ailable or furnished to this Authority in the following language:	, which is:			
		the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).					
		the language of publi	ication of the international application (under Rule 48.3(b)).				
		the language of a tra Rule 55.2 and/or 55.3	nslation furnished for the purposes of international preliminary ex	amination (under			
 With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing: 							
		contained in the inter	mational application in written form.				
		filed together with the	e international application in computer readable form.	• :			
		furnished subsequen	itly to this Authority in written form.				
		furnished subsequen	itly to this Authority in computer readable form.				
		The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.					
		The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.					
4.	The	amendments have re	esulted in the cancellation of:				
		the description,	pages:				
		the claims,	Nos.:				
		the drawings,	sheets:				
5.		This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).					
		(Any replacement sh report.)	neet containing such amendments must be referred to under item	1 and annexed to this			
6.	Add	litional observations, i	f necessary:				

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

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ш.	MOL	n-establishment of opinion w	ıtn reg	ara to nove	ity, inventive step and industrial appl	icability		
1.	. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:							
		1 the entire international application,						
	×	claims Nos. 9,10 (industrial ap	·					
		because:						
	×	the said international application, or the said claims Nos. 9,10 relate to the following subject matter which does not require an international preliminary examination (specify):						
		see separate sheet						
		the description, claims or drawings (indicate particular elements below) or said claims Nos. are so unclear that no meaningful opinion could be formed (specify):						
		the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.						
		no international search report	has be	en establish	ed for the said claims Nos.			
2.	or a	neaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/ mino acid sequence listing to comply with the standard provided for in Annex C of the Administrative ructions:						
		the written form has not been furnished or does not comply with the Standard.						
	Π	the computer readable form has not been furnished or does not comply with the Standard.						
٧.	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement							
1.	Sta	tement						
	Nov	velty (N)	Yes: No:	Claims Claims	1-12			
	Inve	entive step (IS)	Yes: No:	Claims Claims	1-12			
	Ind	ustrial applicability (IA)	Yes: No:	Claims Claims	1-8,11,12.			

2. Citations and explanations

see separate sheet



EXAMINATION REPORT - SEPARATE SHEET

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1- Claims 9-10 relate to subject matter considered by this Authority to be covered by the provisions of Rule 67.1 (iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject matter of these claims, cf. Article 34(4)(a)(i) PCT.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1- Reference is made to the following documents cited in the search report:

d1: WO 9723466 d2: WO 9315062

2- Novelty

Formulae (I) of d1 and d2 appear to overlap with present formula (I). In particular.

- formula (I) of d1 overlaps with present formula (I) when:
- G is N, R2-R6 are H, A is phenyl substituted with CONH2, B is a substituted aromatic, R1 is (C1-C6)-alkyl-B
- formula (I) of d2 overlaps with present formula (I) when:
- G is N, R2-R5 and R7 are H, R6 is aralkyl, Ar is a 6-member carbocyclic aromatic ring substituted by Y, Y is CONR9R10, Z is carboxamide.

However, all the compounds disclosed in d1 and d2 lack at least two of the following features which are always present in the compounds of the invention: the group phenyl(CO)N(Et)2, the group phenyl(CO)NHR2 and the group CH2R1. Hence, present compounds can be regarded as novel since they derive from a multiple selection inside the prior art formulae.

None of the two documents disclose processes according to present claims 11 or 12. Hence, the requirements of Art. 33.2 are met.

- 3- Inventive activity
- 3.1- The applicant has set himself the task of providing novel ligands of δ receptor which can be useful for the treatment of pain and gastrointestinal disorders.



INTERNATIONAL PRELIMINARY

International application No. PCT/SE 03/01703

EXAMINATION REPORT - SEPARATE SHEET

The compounds of d1 are disclosed as ligands of δ receptor useful in the treatment of pain. Also the compounds of d2 bind the opiod receptors, in particular the δ and μ subreceptors.

D1 is taken as the closest prior art.

The data supplied on Table 1 of the application provide the evidence that present compounds selectively bound the δ receptor.

Hence, the objective technical problem can be regarded as the provision of further ligands of δ receptor.

3.2- The solution of this problem, represented by the compounds of formula (I) is regarded as obvious. As already stated above, present formula (I) is included, at least in part in formula (I) of d1. The skilled person, in the absence of any serious reason for doubting of the content of d1 would consider that substantially all the compounds encompassed by the formula (I) of this document possess the claimed activity, i.e. they are ligands of δ receptor. Hence, the mere fact of selecting a novel subclass of \cdot compounds inside the formula (I) of d1 and observing that the compounds of this subclass have the same activity disclosed in d1 for the whole formula (I) cannot be regarded as an activity involving an inventive skill.

The process of claims 11 and 12 are based upon common reactions, such as the alkylation of an amine and the hydrolysis of a nitrile, which are well known in the field of organic chemistry.

Hence, also these claims do not fulfil the requirements of Art. 33.3 PCT.